

We claim:

1. A modified therapeutic agent comprising:
a therapeutic agent and a reactive group which reacts in vivo with
5 amino groups, hydroxyl groups or thiol groups on pulmonary components or
blood components to form a stable covalent bond,
the therapeutic agent being selected from the group consisting of GP-
41 peptides, BBB peptides, anti-cancer agents, antihistamines,
bronchodilators, anti-hypertension agents, anti-angina agents, opioids,
10 analgesics, anti-depressants, and hypothyroid agents.
2. The modified therapeutic agent of claim 1 wherein said reactive group
is a succinimidyl or a maleimido group.
- 15 3. The modified therapeutic agent of claim 1 wherein said reactive group
is a maleimido group which is reactive with a thiol group on a mobile
pulmonary component.
- 20 4. The modified therapeutic agent of claim 1 wherein said reactive group
is a maleimido group which is reactive with a thiol group on a fixed pulmonary
component.
- 25 5. The modified therapeutic agent of claim 1 wherein said reactive group
is a maleimido group which is reactive with a thiol group on a mobile blood
component.
6. The modified therapeutic agent of claim 1 wherein said reactive group
is a maleimido group which is reactive with a thiol group on albumin.
- 30 7. The modified therapeutic agent of claim 1 wherein said reactive group
is a maleimido group which is reactive with a thiol group on a fixed blood
component.
- 35 8. The modified therapeutic agent of claim 1 wherein said therapeutic
agent is an anti-histamine.
9. The modified therapeutic agent of claim 1 wherein said therapeutic
agent is a hypothyroid agent.

10. The modified therapeutic agent of claim 9 wherein said therapeutic agent is loratidine.
- 5 11. The modified therapeutic agent of claim 9 wherein said therapeutic agent is cetirizine.
12. An aerosol composition for delivery of a therapeutic agent to the pulmonary system of a host comprising:
an aerosolized aqueous solution containing a modified therapeutic agent, the modified therapeutic agent comprising a therapeutic agent and a reactive group which reacts with amino groups, hydroxyl groups or thiol groups on pulmonary or blood components to form a stable covalent bond.
- 10 13. The aerosol of claim 12 further comprising a pharmaceutically acceptable carrier.
- 15 14. The aerosol of claim 12 wherein said modified therapeutic agent is 2.5-10% by weight.
- 20 15. The aerosol of claim 12 wherein said therapeutic agent is an anti-histamine.
16. The aerosol of claim 15 wherein said therapeutic agent is loratidine.
- 25 17. The aerosol of claim 15 wherein said therapeutic agent is cetirizine.
18. A particulate formulation for delivery of a therapeutic agent to the pulmonary system of a host comprising:
a dispersible dry powder containing a modified therapeutic agent, the modified therapeutic agent comprising a therapeutic agent and a reactive group which reacts with amino groups, hydroxyl groups or thiol groups on pulmonary components to form a stable covalent bond.
- 30 19. The particulate formulation of claim 18 wherein at least 50% of the dry powder is in the form of particles having a diameter of 10 μ m or less.
- 35 20. The particulate formulation of claim 18 wherein said therapeutic agent is an anti-histamine.

21. The particulate formulation of claim 20 wherein said therapeutic agent is loratidine.
- 5 22. The particulate formulation of claim 20 wherein said therapeutic agent is cetirizine.
23. A method of delivering a therapeutic agent to a host comprising the steps of:
- 10 obtaining a modified therapeutic agent, the modified therapeutic agent comprising a therapeutic agent and a reactive group which reacts in vivo with amino groups, hydroxyl groups or thiol groups on pulmonary or blood components to form a stable covalent bond; and
- administering the modified therapeutic agent to the pulmonary system of the host.
- 15 24. The method of claim 23 wherein said administering step further comprises the steps of aerosolizing the modified therapeutic agent for inhalation by the host.
- 20 25. The method of claim 23 wherein said administering step further comprises the steps of dispersing a dry formulation of the modified therapeutic agent for inhalation by the host.
- 25 26. The method of claim 23 wherein said administering step further comprises the steps of instilling the modified therapeutic agent into the pulmonary system of the host.
27. The method of claim 23 wherein said reactive group is a succinimidyl or a maleimido group.
- 30 28. The method of claim 23 wherein said reactive group is a maleimido group which is reactive with a thiol group on a mobile pulmonary component.
29. The method of claim 23 wherein said reactive group is a maleimido group which is reactive with a thiol group on a fixed pulmonary component.
- 35 30. The method of claim 23 wherein said reactive group is a maleimido group which is reactive with a thiol group on a mobile blood component.

31. The method of claim 23 wherein said reactive group is a maleimido group which is reactive with a thiol group on a fixed blood component.
- 5 32. The method of claim 23 wherein said reactive group is a maleimido group which is reactive with a thiol group on human serum albumin.
33. The method of claim 23 wherein said therapeutic agent is an anti-histamine.
- 10 34. The method of claim 33 wherein said therapeutic agent is loratidine.
35. The method of claim 33 wherein said therapeutic agent is cetirizine.
- 15 36. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an antihistamine and analogs thereof wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anhistamine effect.
- 20 37. Use of a composition according to Claim 36 wherein the antihistamine is selected from cetirizine, loratidine and analogs thereof.
- 25 38. Use of a composition according to Claim 36 wherein the antihistamine is selected from cetirizine and analogs thereof.
- 30 39. Use of a composition according to Claim 36 wherein the antihistamine is selected from loratidine and analogs thereof.
- 35 40. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an anti-angina agent and analogs thereof wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anti-angina effect.

41. Use of a composition according to Claim 40 wherein the anti-angina agent is tirofiban.
- 5 42. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an anti-hypertensive agent and analogs thereof wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anti-hypertensive effect.
- 10 43. Use of a composition according to Claim 42 wherein the anti-hypertensive agent is enalapril.
- 15 44. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an anti-arrhythmic agent and analogs thereof wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anti-arrhythmic effect.
- 20 45. Use of a composition according to Claim 44 wherein the anti-arrhythmic agent is capobenic acid.
- 25 46. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an anti-depressant agent and analogs thereof wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anti-depressant effect.
- 30 47. Use of a composition according to Claim 46 wherein the anti-depressant agent is fluoxetine.
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48. Use of a composition for the manufacture of a medicament said composition comprising a derivative of a bronchodilator and analogs thereof wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide a bronchodilation effect.

49. Use of a composition according to Claim 48 wherein the bronchodilator is theobromineacetamine and analogs thereof.

50. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an anti-inflammatory agent and analogs thereof, wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anti-inflammatory effect.

51. Use of a composition according to Claim 50 wherein the anti-inflammatory agent is loxoprofen and analogs thereof.

52. Use of a composition for the manufacture of a medicament said composition comprising a derivative of an anti-thyroid deficiency agent and analogs thereof, wherein the derivative includes a reactive functional group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds, said reactive functional group being selected from N-hydroxysuccinimide, *N*-hydroxy-sulfosuccinimide and a maleimide group for use in the treatment of the human body to provide an anti-thyroid deficiency effect.

53. Use of a composition according to Claim 52 wherein the anti-thyroid deficiency agent is thyroxin and analogs thereof.

54. A composition comprising a compound selected from the group consisting of:

2-[2-[4-[(4-chlorophenyl)phenylmethyl[1-piperazinyl]ethoxy]-maleimidopropionylacetamide; 11-(N-maleimidopropionyl-4-piperidylidene)-8-chloro-6,11-dihydro-5H-benzo-[5,6]-cyclohepta-[1,2-b]-pyridine; N-(1(S)-Ethoxycarbonyl-3-phenylpropyl)-L-alanyl-L-prolinylmaleimidopropionilamide; Maleimidopropynamyl-ε-(3,4,5-trimethoxybenz-amido)-caproicamide; Maleimidopropionamyl-1-theobromineacetamide; Maleimidopropamyl-2-[4-(2-oxocyclopentan-1-ylmethyl)phenyl]propionamide N-maleimidopropionyl-N-methyl-3-(p-trifluoromethylphenoxy)-3-phenylpropylamine; 4-anilino-1-(2-phenethyl)piperidine and Maleimidopropionamyl-3,5-3',5' tetraiodothyroninamide.

55. The composition of claim 54, wherein the compound is Maleimidopropionamyl-3,5-3',5' tetraiodothyroninamide.

56. An aerosol composition for delivery of a therapeutic agent to the pulmonary system of a host comprising an aerosolized aqueous solution containing a modified therapeutic agent conjugated to a blood protein.

57. The composition of claim 56 wherein said protein is albumin.

58. The aerosol of claim 56 wherein said therapeutic agent is an anti-histamine.

59. The aerosol of claim 56 wherein said therapeutic agent is loratidine.

60. The aerosol of claim 56 wherein said therapeutic agent is cetirizine.

61. A particulate formulation for delivery of a therapeutic agent to the pulmonary system of a host comprising:
a dispersable dry powder containing a modified therapeutic agent, the modified therapeutic agent comprising a therapeutic agent and a reactive group which reacts with amino groups, hydroxyl groups or thiol groups on pulmonary components to form a stable covalent bond wherein said therapeutic agent is covalently bonded to a blood protein.

62. The formulation of claim 61 wherein said protein is albumin.

63. The formulation of claim 61 wherein said therapeutic agent is an anti-histamine.

5 64. The formulation of claim 61 wherein said therapeutic agent is loratidine.

65. The particulate formulation of claim 61 wherein said therapeutic agent is cetirizine.

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